

they may actually be harmful to them and their families (through their effect on beneficial bacteria in the body) and to society at large (through encouraging resistance). All this requires considerable effort and time, not easily achieved in a five minute consultation. The American Academy of Paediatrics has made a start in giving guidance to parents.<sup>6</sup> Advances in rapid diagnosis will help to remove uncertainties.

The coming years will undoubtedly see the introduction of strict clinical guidelines on antibiotic prescribing. At present there is a tendency to concentrate on which antibiotic to use rather than question whether an antimicrobial is useful at all. More firm guidance is also required on the optimum length of treatment. In many parts of the world simple cystitis is still treated for 5-7 days and the more common chest infections for up to 14 days. The drug regulatory authorities therefore have their part to play in insisting that relevant clinical trials support the licence of an antimicrobial.

There is much discussion world wide about surveillance schemes for antimicrobial resistance.<sup>7</sup> The major problem is gaining useful denominator data—that is, how to obtain an accurate picture of resistance in a community, be it in hospital or general practice. In hospital it is moderately straightforward, since ward based surveys can be undertaken, but in general practice we have little accurate information. As resistance rates of common pathogens can vary greatly over short distances,<sup>8</sup> such surveillance must be undertaken both nationally, so that meaningful broad based policies can be devised, and locally, so that relevant clinical guidelines can be developed.

Greater insights are required into how resistance genes spread, especially in the community, where there is a paucity of information. Infection control procedures in child and elderly care units require enhancing. Scientific funding bodies across the European Union should realise that if we are to understand the levers which control antibiotic resistance more fundamental research will require funding. The House of Lords report highlights the problems of funding research in this area of medicine,<sup>5</sup> which in the past has mainly come from the pharmaceutical industry.

Finally, the pharmaceutical industry, which until recently has been ahead of the resistance race, will also be well advised to increase its commitment to

antimicrobial research. Indeed, now that several bacterial genomes have been sequenced, there are signs that this is occurring.<sup>9</sup> In this issue, we trust that these and other matters have been confronted. We wish the European Union medical officers' conference well. The problems they are addressing are real and can be approached only by concerted action as bacteria respect no country's borders. The past decade has seen the progressive intercontinental spread of methicillin resistant *Staphylococcus aureus*<sup>10</sup> and penicillin resistant *Streptococcus pneumoniae*,<sup>11</sup> and there are concerns about increasing resistance of *Salmonella typhi*.<sup>12</sup> Parochial approaches are therefore doomed to failure.

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## Antimicrobial resistance: a veterinary perspective

*Antimicrobials are important for animal welfare but need to be used prudently*

**B**acterial disease is a major constraint on the efficient production of animal derived food and causes ill health and suffering in both food producing and companion animals. In some production systems the spread of bacterial disease may be accelerated by the proximity of the animals. Bacterial disease may be controlled in some situations by eradication, maintenance of animals of specified health status, vaccination, and good hygiene. Nevertheless, antimicrobial chemotherapy remains vitally impor-

tant for treating and in some cases preventing bacterial disease. Many bacterial diseases of animals are potentially fatal; others cause pain and distress. Appropriate use of antimicrobials will cure some sick animals and speed the recovery of others, and may improve the welfare of treated animals and reduce the spread of infection to other animals or, in the case of zoonotic disease, to humans. The challenge is to use antimicrobials wisely, minimising the risk of resistance.

The short generation time and ability to exchange genetic material has inevitably resulted in the development of resistance to antimicrobials by many animal bacteria.<sup>1</sup> Nevertheless, some drugs have retained excellent activity against particular target organisms, such as penicillin against *Streptococcus agalactia* despite extensive use for 40 years.<sup>2</sup> The development of resistance to animal antimicrobials may present a hazard to humans when the resistant bacteria can cause disease in humans and can be transmitted via contaminated food. Bacteria from animals which do not cause human disease may still present a hazard when transferred via food if they then transfer their genetic material coding for resistance to pathogenic human bacteria. Clearly a risk to humans exists when the antimicrobial used in animals is also used in humans or displays cross resistance with an antimicrobial used in human medicine. This risk has not been quantified.

The risk of transfer of antimicrobial resistance from animals to humans could be much reduced if transfer of bacteria could be minimised. One way is more stringent hygiene in markets, abattoirs, and food processing plants. Pasteurisation has very effectively limited transmission in the dairy industry, and irradiation could do the same for other animal derived foodstuffs. Effective cooking by the consumer also reduces the risk.

Clearly antimicrobial resistance would not develop in animals if antimicrobials were not used in animals. But a draconian decision to prohibit their use in animals would devastate the livestock industry, increase bacterial—including zoonotic—disease, and have a catastrophic effect on animal welfare. Nevertheless, particular practices should be scrutinised to ensure that the benefit to animals and to society outweighs the risk.

Antibiotics fed at low, generally subtherapeutic concentrations are known to improve feed conversion efficiency and thus performance in food producing animals. The improvement may reflect a reduction in subclinical disease, although this is probably not the whole reason.<sup>3</sup> In the United Kingdom only antibiotics not used in human medicine and those which do not select for cross resistance with antibiotics used in humans are available for performance enhancement. Furthermore, these antimicrobials are only minimally absorbed after oral administration and thus do not present a risk of residues. Since resistance to the performance enhancing antimicrobial avoparcin may be common with that to vancomycin,<sup>4 5</sup> this drug has recently been withdrawn as a growth promoter in Europe. Furthermore, the potential use of streptogramins in human medicine has resulted in scrutiny of the growth promotant virginicmycin, which may express common resistance.<sup>6</sup>

Prophylactic use of antimicrobials is more common in veterinary practice than in human medicine and reflects husbandry systems where animals are contained in close proximity within the same patch of air or water. Group medication in these circumstances may involve therapeutic treatment of affected animals and prophylactic medication of unaffected contacts. The antimicrobials are administered at therapeutic dosages, which clearly differentiates this strategy from that used to enhance production. Prophylactic use of antimicrobials should be used only when disease spread cannot be contained by vaccination, changes in management, or better hygiene and when the development of disease in

animals in contact with an infected case is virtually inevitable without antimicrobial intervention.

Targeted therapeutic use of an antimicrobial to treat a specific disease in a clinically affected animal presents a rational and justifiable use. The antimicrobial should be selected on the basis of the sensitivity of the infecting organism and the pharmacokinetics of the drug, ensuring attainment of appropriate concentrations at the site of infection. Narrow spectrum agents which affect the fewest commensal bacteria should be used and the drug administered in the most effective dosage.

Currently little information exists on optimal administration strategies for antimicrobials in animals or humans.<sup>7</sup> Since exposure of bacteria to subtherapeutic concentrations of antimicrobials is thought to increase the speed of selection of resistance, this should be avoided.<sup>8</sup> Appropriate pharmacokinetic-pharmacodynamic relations for antimicrobials used in animals should be developed. Bacteria develop resistance to some antimicrobials by chromosomal mutation, not by acquisition of genetic material from other bacteria, and when these drugs are used resistance in animals will prove a hazard to humans only for zoonotic bacteria. Optimal dosage strategies for eliminating zoonotic organisms in animals will thus reduce the risk of transferring resistance to humans. For other antimicrobials, however, bacteria develop plasmid mediated transferable resistance, and when these are used in animals optimising dosage strategies may prove more difficult. The minimum inhibitory concentrations (and thus dosage strategy) required for the target pathogen might differ substantially from those of commensal organisms. Genetic material coding for resistance in commensal organisms may thus be selected and transferred to humans and then to human pathogenic organisms. Nevertheless, even for these antimicrobials, optimal dosage strategies will expose commensal bacteria to the minimum selective pressure and should be encouraged.

Antimicrobials are an extremely valuable resource in livestock production. Their prudent use in animals will continue to provide benefits to society and will help ensure high standards of welfare for those animals in our care.

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